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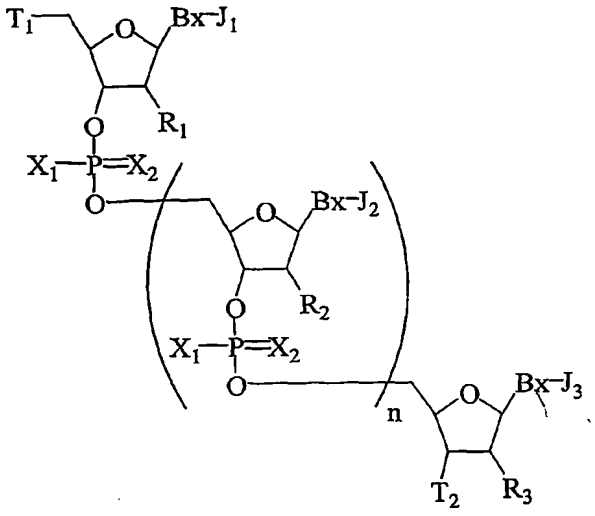
(54) Title: OLIGOMERIC COMPOUNDS HAVING MODIFIED PHOSPHATE GROUPS

(57) Abstract: Oligomeric compounds having at least one phosphorothioate monoester are provided having increased nuclease resistance and binding affinity to a complementary strand of nucleic acid. Such oligomeric compounds are useful for diagnostics and other research purposes, for modulating the expression of a protein in organisms, and for the diagnosis, detection and treatment of other conditions responsive to oligonucleotide therapeutics.

AMENDED CLAIMS

**[Received by the International Bureau on 06 October 2004 (06.10.04)
original claims 1 and 24 amended;
remaining claims unchanged (8 pages)].**

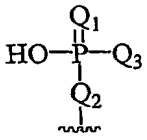
1 (amended). An oligomeric compound having the formula:



wherein:

each Bx is, independently, a heterocyclic base moiety;

J_1, J_3 and each J_2 is, independently, hydrogen or a modified phosphate group having the structure:



wherein

one of Q_1 and Q_2 is S and the other of Q_1 and Q_2 is O;

Q_3 is OH or CH_3;

R_1, R_3 and each R_2 is, independently, hydrogen, hydroxyl, a sugar substituent group a protected sugar substituent group or said modified phosphate group;

each T_1 and T_2 is, independently, hydroxyl, a protected hydroxyl, an oligonucleotide, an oligonucleoside or said modified phosphate group;

each X_1 and X_2 is, independently, O or S wherein at least one X_1 is S;

n is from 3 to 48; and

wherein at least one of J_1, J_2, J_3, ~~R_1, R_2, R_3,~~ T_1 or T_2 is said modified phosphate group.

2 (original). The oligomeric compound of claim 1 wherein Q_1 is S.

3 (original). The oligomeric compound of claim 1 wherein Q_2 is S.

4 (original). The oligomeric compound of claim 1 wherein Q_3 is CH_3.

5 (original). The oligomeric compound of claim 1 wherein J_1 is said modified phosphate group.

6 (original). The oligomeric compound of claim 1 wherein at least one J_2 is said modified phosphate group.

7 (original). The oligomeric compound of claim 1 wherein J_3 is said modified phosphate group.

8 (original) The oligomeric compound of claim 1 wherein R_1 is a modified phosphate group.

9 (original). The oligomeric compound of claim 1 wherein at least one R_2 is a modified phosphate group.

10 (original). The oligomeric compound of claim 1 wherein R_3 is a modified phosphate group.

11 (original). The oligomeric compound of claim 1 wherein R_1, R_3 and each R_2 is hydrogen.

12 (original). The oligomeric compound of claim 1 wherein R_1, R_3 and each R_2 is hydroxyl.

13 (original). The oligomeric compound of claim 1 wherein R_1, R_3 and each R_2 is hydrogen, hydroxyl a sugar substituent group or a protected sugar substituent group.

14 (original). The oligomeric compound of claim 1 wherein at least one of R_1, R_2 or R_3 is an optionally protected sugar substituent group.

15 (original). The oligomeric compound of claim 1 wherein each X_2 is S.

16 (original). The oligomeric compound of claim 1 wherein each heterocyclic base moiety is, independently, adenine, cytosine, 5-methylcytosine, thymine, uracil, guanine or 2-aminoadenine.

17 (original). The oligomeric compound of claim 1 wherein n is from about 8 to about 30.

18 (original). The oligomeric compound of claim 1 wherein n is from about 15 to 25.

19 (original). A method of treating an organism having a disease characterized by the undesired production of a protein comprising contacting the organism with an oligomeric compound of claim 1.

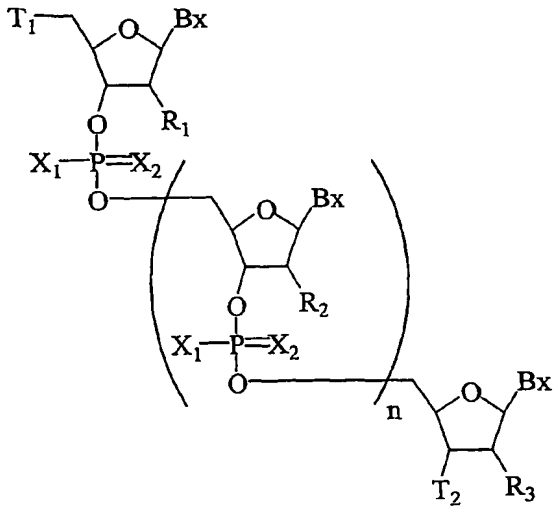
20 (original). A pharmaceutical composition comprising:
a pharmaceutically effective amount of an oligomeric compound of claim 1; and
a pharmaceutically acceptable diluent or carrier.

21 (original). A method of modifying *in vitro* a nucleic acid, comprising contacting a test solution containing RNase H and said nucleic acid with an oligomeric compound of claim 1.

22 (original). A method of concurrently enhancing hybridization and RNase H activation in a organism comprising contacting the organism with an oligomeric compound of claim 1.

23 (original). A method comprising contacting a cell with an oligomeric compound of claim 1.

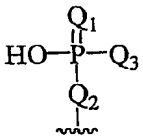
24 (currently amended). An oligomeric compound having the formula:



wherein

each Bx is, independently, a heterocyclic base moiety;

each T_1 and T_2 is, independently, hydroxyl, a protected hydroxyl, an oligonucleotide, an oligonucleoside or a modified phosphate group having the formula;



wherein

one of Q_1 and Q_2 is S and the other of Q_1 and Q_2 is O;

Q_3 is OH or CH_3;

R_1, R_3 and each R_2 is, independently, hydrogen, hydroxyl, a sugar substituent group, or a protected sugar substituent group;

each X_1 and X_2 is, independently, O or S wherein at least one X_1 is S; and

n is from 3 to 48;

wherein at least one of X_1, X_2, J_1, J_2, and J_3 is said modified phosphate group.

25 (original). The oligomeric compound of claim 24 wherein Q_1 is S.

26 (original). The oligomeric compound of claim 24 wherein Q_2 is S.

27 (original). The oligomeric compound of claim 24 wherein Q_3 is CH_3.

28 (original). The oligomeric compound of claim 24 wherein J_1 is said modified phosphate group.

29 (original). The oligomeric compound of claim 24 wherein at least one J_2 is a modified phosphate group.

30 (original). The oligomeric compound of claim 24 wherein J_3 is said modified phosphate group.

31 (original). The oligomeric compound of claim 24 wherein R_1 is a modified phosphate group.

32 (original). The oligomeric compound of claim 24 wherein at least one R_2 is a modified phosphate group.

33 (original). The oligomeric compound of claim 24 wherein R_3 is a modified phosphate group.

34 (original). The oligomeric compound of claim 24 wherein R_1, R_3 and each R_2 is hydrogen.

35 (original). The oligomeric compound of claim 24 wherein R_1, R_3 and each R_2 is hydroxyl.

36 (original). The oligomeric compound of claim 24 wherein R_1, R_3 and each R_2 is hydrogen, hydroxyl a sugar substituent group or a protected sugar substituent group.

37 (original). The oligomeric compound of claim 24 wherein at least one of R_1, R_2 or R_3 is an optionally protected sugar substituent group.

38 (original). The oligomeric compound of claim 24 wherein each X_2 is S.

39 (original). The oligomeric compound of claim 24 wherein each heterocyclic base moiety is, independently, adenine, cytosine, 5-methylcytosine, thymine, uracil, guanine or 2-aminoadenine.

40 (original). The oligomeric compound of claim 24 wherein n is from about 8 to about 30.

41 (original). The oligomeric compound of claim 24 wherein n is from about 15 to 25.

STATEMENT UNDER PCT ARTICLE 19

In response to the International Search Report mailed 10 September 2004, for the above-identified International Patent Application, enclosed is an Amendment Under Article 19. Sheets numbered 96 and 99 are enclosed to replace originally submitted sheets 96 and 99 of the claims.

Claims 1 and 24 are amended in the replacement sheets. The basis for the amendments can be found, for example, at page 10, lines 5-7 of the paragraph immediately above paragraph 26.